

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 46684.WO01	FOR FURTHER ACTION	See item 4 below
International application No. PCT/GB2004/005092	International filing date (<i>day/month/year</i>) 03 December 2004 (03.12.2004)	Priority date (<i>day/month/year</i>) 05 December 2003 (05.12.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant CAMBRIDGE BIOTECHNOLOGY LIMITED		

1.	This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).																								
2.	This REPORT consists of a total of 7 sheets, including this cover sheet. In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.																								
3.	<p>This report contains indications relating to the following items:</p> <table style="width: 100%; border: none;"> <tr> <td style="width: 10%; text-align: center;"><input checked="" type="checkbox"/></td> <td style="width: 30%;">Box No. I</td> <td style="width: 60%;">Basis of the report</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input checked="" type="checkbox"/>	Box No. VIII	Certain observations on the international application
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4.	The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).																								

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 740 14 35	<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border-bottom: 1px solid black;">Date of issuance of this report 07 June 2006 (07.06.2006)</td> <td style="width: 50%;"></td> </tr> <tr> <td style="border-bottom: 1px solid black;">Authorized officer Nora Lindner</td> <td></td> </tr> <tr> <td style="border-bottom: 1px solid black;">Telephone No. +41 22 338 89 65</td> <td></td> </tr> </table>	Date of issuance of this report 07 June 2006 (07.06.2006)		Authorized officer Nora Lindner		Telephone No. +41 22 338 89 65	
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PATENT COOPERATION TREATY

REC'D 25 MAY 2005

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From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2004/005092

International filing date (day/month/year)
03.12.2004

Priority date (day/month/year)
05.12.2003

International Patent Classification (IPC) or both national classification and IPC
C07H19/167

Applicant
CAMBRIDGE BIOTECHNOLOGY LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/005092

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/005092

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 32,33,35,37,38

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 32,33,35,37,38 are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/005092

**Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or
Industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-31,40
	No: Claims	34,36,39
Inventive step (IS)	Yes: Claims	1-31
	No: Claims	40
Industrial applicability (IA)	Yes: Claims	1-31,34,36,39,40
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the International application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The claims 32, 33, 35 do not specify the technical features of the invention (Rule 6.2 (a) PCT).

The use claims 37 and 38 define neither the reagents nor the reaction steps required to perform the synthesis of compound (I) or (II).

An examination of these claims is not possible.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Spongosine and its derivatives as claimed in claim 34 are comprised in the prior art, see D1/ J. Med. Chem. 34, 1334 (1991), table I. The intermediates of formula (II) as claimed in claim 36 are also not new in the light of D2/ J. Org. Chem. 31, 3258 (1966) (compound XII) and D3/ J. Am. Chem. Soc. 80, 3738 (1958) (compound VII).

Claim 39 is not clearly distinguished over the known method to nitrate a substituted adenosine as disclosed in D4/ Tetrahedr. Lett. 41, 1291 (2000) by the claim feature "reducing the amount of TBA or TMA impurities contaminating the substituted adenosine". Although the recovery of the nitrated adenosine is not disclosed in detail in the reference, it is evident that the recovery of the product forms part of the known synthesis. The isolation of the product leads to a reduction of the amount of contaminating TBA in the final product. The subject-matter of claim 39 therefore lacks novelty.

Claim 40 specifies the purification of the nitrated adenosine after synthesis. The steps mentioned in the claim are based on generally applicable methods to purify an organic compound (trituration, washing with solvents). The product yield is lower than in the reference due to the washing steps (58% in step 3 - 71% according to the reference). A

skilled person would expect that the product yield will be decreased by the washing steps. In the absence of any surprising effect inventive step cannot be acknowledged.

2. The method of claim 1 to prepare spongiosine and its derivatives is novel over the prior art since a compound of formula (II) is not used as an intermediate for spongiosine in the state of the art (compare D1 which uses a 2-chloroadenosine derivative; D5/ Nucleosides, Nucleotides 14, 1889 (1995) using a 2-sulfone derivative of adenosine).

The applicants demonstrated that according to their method high yields of spongiosine are obtained. Since the prior art does not disclose reactions immediately comparable with the method of claim 1 the usefulness of the claimed synthesis could not have been expected at the filing date of the application. The method of claim 1 therefore possess inventive step.

Re Item VIII

Certain observations on the international application

Claim 1 lacks clarity since it only defines the starting material and the product without indicating the other reagents needed for the synthesis.

Similar objections apply to claims 9, 15, 22, 27.

The abbreviations used in claims 39 and 40 are not self-explanatory and render the claim language unclear.